For Fig 4 Only

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FILE 'HOME' ENTERED AT 23:41:49 ON 05 OCT 2003

=> s ribozyme? or (enzymati? (n) nucle?)
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
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=> FIL MEDLINE BIOSIS EMBASE CA SCISEARCH
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FULL ESTIMATED COST                                       0.63       0.63

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FILE 'SCISEARCH' ENTERED AT 23:43:50 ON 05 OCT 2003
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=> s ribozyme? or (enzymati? (n) nucle?)
L1       21369 RIBOZYME? OR (ENZYMATI? (N) NUCLE?)

=> s hepatit? (n) c (n) vir?
L2       83714 HEPATIT? (N) C (N) VIR?

=> s l1 and l2
L3         366 L1 AND L2

=> s l2 (s) l3
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7  (S) L13'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L8  (S) L14'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L9  (S) L15'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L10 (S) L16'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L11 (S) L17'
L4         366 L2 (S) L3

=> s l2 (s) l1
L5         224 L2 (S) L1

=> s l2 (5n) l1
L6         131 L2 (5N) L1

=> dup rem l6
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PROCESSING COMPLETED FOR L6
L7 83 DUP REM L6 (48 DUPLICATES REMOVED)

=> s l7 and py<=2000
2 FILES SEARCHED...
L8 55 L7 AND PY<=2000

=> d l8 1-55 ibib abs

L8 ANSWER 1 OF 55 MEDLINE on STN
ACCESSION NUMBER: 2000427884 MEDLINE
DOCUMENT NUMBER: 20417956 PubMed ID: 10960462
TITLE: Pharmacokinetics and tissue distribution of a **ribozyme** directed against **hepatitis C virus** RNA following subcutaneous or intravenous administration in mice.
AUTHOR: Lee P A; Blatt L M; Blanchard K S; Bouhana K S; Pavco P A; Bellon L; Sandberg J A
CORPORATE SOURCE: Ribozyme Pharmaceuticals Inc., Boulder, CO 80301, USA.
SOURCE: HEPATOLOGY, **(2000 Sep)** 32 (3) 640-6.
Journal code: 8302946. ISSN: 0270-9139.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914

AB A nuclease resistant ribozyme targeting the 5' untranslated region (5' UTR) of hepatitis C virus (HCV) at site 195 has been identified. To investigate the therapeutic utility of this ribozyme, we evaluated the pharmacokinetics and tissue distribution with two labeled forms of this ribozyme. [(32)P]-labeled ribozyme was administered as a single subcutaneous (SC) or intravenous (IV) bolus at a dose of 10 mg/kg or 30 mg/kg in C57Bl/6 mice. Regardless of route of administration, peak liver concentrations achieved were greater than the concentration necessary to inhibit HCV-IRES-luciferase expression in cell culture. The ribozyme was well absorbed after SC administration (89%) and had an elimination half-life of 23 minutes. To show intracellular localization of the ribozyme in target tissue, a tetramethyl rhodamine (TMR)-labeled ribozyme was administered as a single SC or IV bolus at a dose of 30 mg/kg in C57Bl/6 mice. Mice treated SC or IV with TMR-labeled ribozyme had positive fluorescence in the liver from 15 minutes to 48 hours after dosing. Definite positive fluorescence was still present at 72 hours in the mice dosed via the IV route. At early time points (15 and 30 minutes postinjection), nuclear and possibly cytoplasmic fluorescence was present in the hepatocytes, and sinusoidal fluorescence was intense. At the later time points, fluorescence became more punctate. Abundant staining was often present in Kupffer cells. This study confirms the retention of ribozyme in liver cells and supports the potential of an anti-HCV ribozyme as a therapeutic agent for treatment of chronic hepatitis C.

L8 ANSWER 2 OF 55 MEDLINE on STN
ACCESSION NUMBER: 2000172032 MEDLINE
DOCUMENT NUMBER: 20172032 PubMed ID: 10706571
TITLE: Inhibition of hepatitis C virus (HCV)-RNA-dependent translation and replication of a chimeric HCV poliovirus using synthetic stabilized ribozymes.
AUTHOR: Macejak D G; Jensen K L; Jamison S F; Domenico K; Roberts E C; Chaudhary N; von Carlowitz I; Bellon L; Tong M J; Conrad A; Pavco P A; Blatt L M

CORPORATE SOURCE: Ribozyme Pharmaceuticals Incorporated, Boulder, CO 80301, USA.
SOURCE: HEPATOLOGY, **(2000 Mar)** 31 (3) 769-76.
Journal code: 8302946. ISSN: 0270-9139.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000315

AB Ribozymes are catalytic RNA molecules that can be designed to cleave specific RNA sequences. To investigate the potential use of synthetic stabilized **ribozymes** for the treatment of chronic **hepatitis C virus** (HCV) infection, we designed and synthesized hammerhead ribozymes targeting 15 conserved sites in the 5' untranslated region (UTR) of HCV RNA. This region forms an internal ribosome entry site that allows for efficient translation of the HCV polyprotein. The 15 synthetic ribozymes contained modified nucleotides and linkages that stabilize the molecules against nuclease degradation. All 15 ribozymes were tested for their ability to reduce expression in an HCV 5' UTR/luciferase reporter system and for their ability to inhibit replication of an HCV-poliovirus (HCV-PV) chimera. Treatment with several ribozymes resulted in significant down-regulation of HCV 5' UTR/luciferase reporter expression (range 40% to 80% inhibition, P <.05). Moreover, several ribozymes showed significant inhibition (>90%, P <.001) of chimeric HCV-PV replication. We further show that the inhibitory activity of ribozymes targeting site 195 of HCV RNA exhibits a sequence-specific dose response, requires an active catalytic ribozyme core, and is dependent on the presence of the HCV 5' UTR. Treatment with synthetic stabilized anti-HCV ribozymes has the potential to aid patients who are infected with HCV by reducing the viral burden through specific targeting and cleavage of the viral genome.

L8 ANSWER 3 OF 55 MEDLINE on STN
ACCESSION NUMBER: 2000017547 MEDLINE
DOCUMENT NUMBER: 20017547 PubMed ID: 10551385
TITLE: Inhibition of hepatitis C virus-directed gene expression by a DNA ribonuclease.
AUTHOR: Oketani M; Asahina Y; Wu C H; Wu G Y
CORPORATE SOURCE: Department of Medicine, University of Connecticut Health Center, Farmington 06030, USA.
CONTRACT NUMBER: DK-42182 (NIDDK)
SOURCE: JOURNAL OF HEPATOLOGY, **(1999 Oct)** 31 (4) 628-34.
Journal code: 8503886. ISSN: 0168-8278.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991206

AB BACKGROUND/AIMS: The aim of this study was to determine whether DNA analogs of **ribozymes** could be prepared to inhibit **hepatitis C virus** (HCV) gene expression.
METHODS: Two DNA ribonucleases, Dz2 and Dz4, were designed with varying arm lengths, to cleave at the 5'-noncoding region (NCR) just upstream from the translation start site, and core region of HCV genome, respectively. A reporter vector was prepared to contain target HCV regulatory sequences controlling a downstream luciferase gene. DNA ribonucleases with normal

phosphodiester, as well as with terminal phosphorothioate linkages, were administered to Huh7 cells, and luciferase activity was measured. RESULTS: DNA ribonucleases were highly active in cleaving HCV RNA targets. Enzymes with longer arms had consistently higher cleavage activity compared to enzymes with shorter arms under cell-free conditions. Furthermore, in Huh7 cells, terminal phosphorothioate derivatives, Dz2 and Dz4, significantly suppressed HCV-luciferase fusion gene expression up to 45% and 67% of controls, respectively. Interestingly, phosphorothioate-modified DNA ribonucleases had greater inhibitory effects on target gene expression than their unmodified counterparts. In contrast, DNA ribonucleases with point mutations in the catalytic domain had significantly lower inhibitory effects compared to wild-type DNA ribonucleases. However, activity was not eliminated, suggesting that some antisense contribution was present. CONCLUSIONS: DNA ribonucleases directed against the HCV genome can specifically cleave target HCV RNA. Modifications of the extreme 3'- and 5'-termini protect against nuclease degradation without appreciable reduction in inhibitory activity against viral gene expression under intracellular conditions.

L8 ANSWER 4 OF 55 MEDLINE on STN
ACCESSION NUMBER: 1998412673 MEDLINE
DOCUMENT NUMBER: 98412673 PubMed ID: 9741642
TITLE: **Ribozyme** gene therapy for **hepatitis C virus** infection.
AUTHOR: Welch P J; Yei S; Barber J R
CORPORATE SOURCE: Immusol Inc., San Diego, CA 92121, USA.
SOURCE: CLINICAL AND DIAGNOSTIC VIROLOGY, **(1998 Jul 15)** 10 (2-3) 163-71.
Journal code: 9309653. ISSN: 0928-0197.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981208

AB BACKGROUND: The development of antiviral drugs for hepatitis C virus (HCV) infection represents a substantial challenge. Similar to human immunodeficiency virus (HIV), HCV is highly prone to mutation. It is, therefore, expected that potential HCV therapeutics currently under development, such as protease inhibitors, will suffer from the same shortcomings of HIV therapeutic drugs; the emergence of drug resistant viral mutants. Ribozymes (Rz) are enzymatic RNA molecules that can be engineered to specifically target any given RNA molecule. A therapeutic Rz can be manufactured and administered as a drug, or a Rz gene can be delivered and expressed intracellularly by gene therapy. For HCV therapeutics, we favour the gene therapy approach as delivery and in vivo expression of Rz genes will result in a constant and continuous supply of multiple intracellular Rz, offering less opportunity for the development of drug-resistant viral variants. OBJECTIVES: To utilise direct intravenous injection of hepatotropic viral vectors to transfer Rz genes directly into the hepatocytes of HCV-infected patients, resulting in degradation of the HCV positive strand RNA genome, the viral mRNAs, and even the negative strand RNA replication intermediate. We plan to circumvent the emergence of drug-resistant viral mutants by targeting multiple, highly conserved HCV RNA sequences simultaneously with multiple Rz genes expressed from a single vector. STUDY DESIGN: Rzs targeting conserved regions of the HCV positive and negative RNAs were transcribed in vitro and used to cleave HCV target RNAs. The most effective Rzs identified were then incorporated into adeno associated viral (AAV) vectors and adenoviral (AV) vectors and tested for their ability to

inhibit HCV core expression in a tissue culture model. RESULTS: Several Rzs targeting highly conserved HCV sequences effectively degraded positive and negative strands of HCV RNA in vitro. Furthermore, substantial inhibition of HCV gene expression was observed in tissue culture using viral vectors to deliver and express Rz genes. CONCLUSIONS: Rz gene therapy has potential for the production of anti-viral drugs directed against HCV. Initial studies employing Rz gene therapy to produced anti-viral drugs against HCV have proved successful. Rz gene therapy may be a useful approach to overcome problems associated with anti-HCV drug design, such as the emergence of drug-resistant mutants.

L8 ANSWER 5 OF 55 MEDLINE on STN
ACCESSION NUMBER: 97394359 MEDLINE
DOCUMENT NUMBER: 97394359 PubMed ID: 9252077
TITLE: Cleavage of viral RNA and inhibition of viral translation by **hepatitis C virus** RNA-specific hammerhead **ribozyme** in vitro.
AUTHOR: Ohkawa K; Yuki N; Kanazawa Y; Ueda K; Mita E; Sasaki Y; Kasahara A; Hayashi N
CORPORATE SOURCE: First Department of Medicine, Osaka University School of Medicine, Suita, Japan.
SOURCE: JOURNAL OF HEPATOLOGY, **(1997 Jul)** 27 (1) 78-84. Journal code: 8503886. ISSN: 0168-8278.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971008
Last Updated on STN: 19971008
Entered Medline: 19970925

AB BACKGROUND/AIMS: A hammerhead ribozyme has been used as a new way to suppress specific gene expression. We designed hammerhead **ribozymes** directed against **hepatitis C virus** RNA, and investigated their cleavage efficiency and inhibitory effect on viral translation in vitro. METHODS: Three hammerhead ribozymes bearing different cleavage sites in the core region of hepatitis C virus RNA (genotype 1b) were designed in this study. **Ribozymes** and the target **hepatitis C virus** RNA were synthesized by in vitro transcription. The cleavage efficiency was evaluated by the ribozyme cleavage assay. The inhibitory effect of the ribozyme on viral translation was further studied by the viral translation inhibition assay. RESULTS: All ribozymes specifically cleaved the target RNA of 1217 bases at a physiological temperature in a dose-dependent manner, with the specific cleavage increasing with a longer incubation period. The target RNA was cleaved most efficiently by the ribozyme with the cleavage site located nearest to the initiation codon. In the viral translation inhibition assay, all ribozymes showed a significant inhibitory effect on viral translation. The ribozyme with the cleavage site located farthest from the initiation codon blocked viral translation most efficiently, and demonstrated almost 70 to 80% inhibition. For ribozymes with the T7 transcription terminator sequence, both the target RNA cleavage and the inhibition of viral translation tended to be achieved less efficiently by ribozymes with T7 terminator than by those without it. CONCLUSIONS: These findings suggest that **ribozyme**-mediated **hepatitis C virus** RNA cleavage may serve as a new strategy in the treatment of hepatitis C virus infection.

L8 ANSWER 6 OF 55 MEDLINE on STN
ACCESSION NUMBER: 97136516 MEDLINE
DOCUMENT NUMBER: 97136516 PubMed ID: 8981917

TITLE: Intracellular cleavage of hepatitis C virus RNA and inhibition of viral protein translation by hammerhead ribozymes.
AUTHOR: Sakamoto N; Wu C H; Wu G Y
CORPORATE SOURCE: Department of Medicine, Division of Gastroenterology-Hepatology, University of Connecticut School of Medicine, Farmington 06030, USA.
CONTRACT NUMBER: DK-42182 (NIDDK)
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, **(1996 Dec 15)** 98 (12) 2720-8.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970130

AB To determine the effects of hammerhead **ribozymes** against **hepatitis C virus** (HCV) RNA on viral protein translation, a luciferase reporter gene vector, pCMV/T7-NCRCdelta-luc, was constructed containing the 5'-noncoding region (5'-NCR) and part of the core region of HCV. Four ribozymes, Rz1-Rz4, were designed to cleave at nucleotide positions 136-160, 313-337, 496-520, and 373-388, respectively. Each ribozyme cleaved the target RNA at expected positions under cell-free conditions. Rz2 and Rz4 significantly suppressed translation of NCRCdelta-luc RNA by 71 and 49%, respectively. Translation of control luciferase mRNA lacking viral elements was not affected by the ribozymes. Furthermore, when NCRCdelta-luc RNA and ribozymes were cotransfected into cells, Rz2 and Rz4 significantly suppressed expression by 73 and 56%, respectively. In contrast, cleavage-deficient ribozymes with a point mutation in the hammerhead domain had no significant effect. To determine the effects of endogenously produced ribozymes, eukaryotic expression vectors for Rz2 and Rz4 were constructed. Cotransfection of the vectors with CMV/T7-NCRCdelta-luc showed suppression of luciferase activities to 50 and 61%, respectively. Moreover, transfection of pCMV/T7-NCRCdelta-luc into stable Rz2 and Rz4 producer cells also showed substantial inhibition of luciferase activity. Ribozymes directed against the HCV genome can substantially and specifically inhibit viral gene expression under intracellular conditions.

L8 ANSWER 7 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:239631 BIOSIS
DOCUMENT NUMBER: PREV200100239631
TITLE: Ribozymes for treating hepatitis C.
AUTHOR(S): Kay, Mark A.; Lieber, Andre
ASSIGNEE: University of Washington
PATENT INFORMATION: US 6107028 August 22, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (**Aug. 22, 2000**) Vol. 1237, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB A method of inhibiting hepatitis C virus RNA replication or expression is provided. The method consists of introducing two or more **ribozymes** specific for **hepatitis C virus** RNA into a cell infected with **hepatitis C virus**. The **ribozymes** specific for **hepatitis C virus** RNA can specifically cleave hepatitis C RNA in a HCV 5' non-coding sequence, the capsid sequence, the NS-5 sequence or any other

conserved region of the hepatitis C RNA. The ribozymes can also be selected so as to be specific for opposite strands of the virus genome. A method of inhibiting hepatitis C virus RNA replication or expression is also provided which consists of introducing into a cell infected with **hepatitis C virus** at least one **ribozyme** specific for **hepatitis C virus** which is selected from the group consisting of GGGAGGTCTCGTAGA [SEQ ID NO: 1], GCACCATGAGCACGA [SEQ ID NO: 2], CCCACAGGACGTCAA [SEQ ID NO: 3], CAACCGTCGCCCACA [SEQ ID NO: 4], TAAACCTCAAAGAAA [SEQ ID NO: 5] GTAAGGTCATCGATA [SEQ ID NO: 6]. Compositions consisting of two or more **ribozymes** specific for **hepatitis C virus** RNA is also provided.

L8 ANSWER 8 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:204752 BIOSIS
DOCUMENT NUMBER: PREV200100204752
TITLE: Ribozymes for treating hepatitis C.
AUTHOR(S): Kay, Mark A. (1); Lieber, Andre
CORPORATE SOURCE: (1) Seattle, WA USA
ASSIGNEE: University of Washington
PATENT INFORMATION: US 6107027 August 22, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (**Aug. 22, 2000**) Vol. 1237, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Adenoviral vectors are used for high efficiency transduction of **ribozymes** specific for **hepatitis C virus** RNA. Hepatocytes are transduced with a recombinant adenovirus vector that expresses a ribozyme capable of specifically cleaving HCV RNA. The compositions and methods thus provide new means for treating HCV, and further provide transgenic non-human animals having human hepatocytes which are useful in models of HCV disease for developing therapeutic and preventative agents.

L8 ANSWER 9 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:507646 BIOSIS
DOCUMENT NUMBER: PREV200000507646
TITLE: Single-dose safety and pharmacokinetics of LY466700, a synthetic nuclease-resistant anti-HCV ribozyme, in healthy adult subjects.
AUTHOR(S): Turik, Michael A. (1); DeSante, Karl A. (1); Hillgren, Kathleen M.; Braun, Daniel K.; Sandberg, Jennifer A.; Gonzales, Celedon R.; LaBell, Elizabeth S.; Ernest, Charles S.; Brown-Augsburger, Patricia L.; Blatt, Lawrence M.
CORPORATE SOURCE: (1) Lilly Lab for Clin Research, Indianapolis, IN USA
SOURCE: Hepatology, (**October, 2000**) Vol. 32, No. 4 Pt. 2, pp. 443A. print.
Meeting Info.: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA October 27-31, 2000 American Association for the Study of Liver Diseases
. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 10 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:337751 BIOSIS
DOCUMENT NUMBER: PREV200000337751
TITLE: Antisense oligonucleotide and **ribozyme** gene

therapy for **hepatitis C virus** infection.
AUTHOR(S): Chen Zhi (1)
CORPORATE SOURCE: (1) Institute of Infectious Disease, Medical College of Zhejiang University, Hangzhou China
SOURCE: Journal of Gastroenterology and Hepatology, (**Dec., 1999**) Vol. 14, No. Suppl. A, pp. A263. print.
Meeting Info.: Second International Symposium on Hepatology Beiging, China December 05-09, 1999
ISSN: 0815-9319.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 11 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:326752 BIOSIS
DOCUMENT NUMBER: PREV200000326752
TITLE: Intracellular inhibition of the viral gene expression by hammerhead **ribozymes** against **hepatitis C virus**.
AUTHOR(S): Jia Zhansheng (1); Zhou Yongxing (1); Lian Jianqi (1)
CORPORATE SOURCE: (1) Department of Infectious Diseases, Tangdu Hospital, Fourth Military Medical University, Xi'an China
SOURCE: Journal of Gastroenterology and Hepatology, (**Dec., 1999**) Vol. 14, No. Suppl. A, pp. A344. print.
Meeting Info.: Second International Symposium on Hepatology Beiging, China December 05-09, 1999
ISSN: 0815-9319.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 12 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:282161 BIOSIS
DOCUMENT NUMBER: PREV200000282161
TITLE: A study of **ribozyme** against **hepatitis C virus** in vitro.
AUTHOR(S): Chen Zhi (1); Liu Yong; Liu Kezhou (1); Dennin, R. H.; Dou Jun (1); Reinhard, U.
CORPORATE SOURCE: (1) The Institute of Infectious Diseases, Zhejiang Medical University, Hangzhou, 310003 China
SOURCE: Chinese Medical Journal (English Edition), (**February, 2000**) Vol. 113, No. 2, pp. 123. print.
ISSN: 0366-6999.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 13 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:513338 BIOSIS
DOCUMENT NUMBER: PREV199900513338
TITLE: Tissue distribution of a **ribozyme** directed against **hepatitis C virus** RNA following subcutaneous or intravenous administration in mice.
AUTHOR(S): Lee, P. A. (1); Blanchard, K. S. (1); Pavco, P. A. (1); Sandberg, J. A. (1); Bellon, L. (1); Blatt, Lawrence M. (1); Chlipala, E.; Bendele, A. M.
CORPORATE SOURCE: (1) Ribozyme Pharmaceuticals, Boulder, CO USA
SOURCE: Hepatology, (**Oct., 1999**) Vol. 30, No. 4 PART 2, pp. 262A.
Meeting Info.: 50th Annual Meeting and Postgraduate Courses

of the American Association for the Study of Liver Diseases Dallas, Texas, USA November 5-9, 1999 American Association for the Study of Liver Diseases
. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 14 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:504477 BIOSIS
DOCUMENT NUMBER: PREV199900504477
TITLE: Optimization of synthetic stabilized **ribozymes** directed against **hepatitis C virus** RNA.
AUTHOR(S): Jamison, S. F. (1); Van Carlowitz, I. R. (1); Macejak, D. G. (1); Pavco, P. A. (1); Roberts, E. C. (1); Bellon, L. (1); Blatt, Lawrence M. (1)
CORPORATE SOURCE: (1) Ribozyme Pharmaceuticals, Boulder, CO USA
SOURCE: Hepatology, (**Oct., 1999**) Vol. 30, No. 4 PART 2, pp. 441A.
Meeting Info.: 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA November 5-9, 1999 American Association for the Study of Liver Diseases
. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 15 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:486792 BIOSIS
DOCUMENT NUMBER: PREV199900486792
TITLE: Inhibition of viral replication by nuclease resistant hammerhead **ribozymes** directed against **hepatitis C virus** RNA.
AUTHOR(S): Macejak, D. J. (1); Jensen, K. L. (1); Bellon, L. (1); Pavco, P. A. (1); Blatt, Lawrence M. (1)
CORPORATE SOURCE: (1) Ribozyme Pharmaceuticals, Boulder, CO USA
SOURCE: Hepatology, (**Oct., 1999**) Vol. 30, No. 4 PART 2, pp. 409A.
Meeting Info.: 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA November 5-9, 1999 American Association for the Study of Liver Diseases
. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 16 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:525898 BIOSIS
DOCUMENT NUMBER: PREV199800525898
TITLE: Synthesis and testing of nuclease resistant hammerhead **ribozymes** directed against **hepatitis C virus** RNA.
AUTHOR(S): Roberts, E. C. (1); Malmstrom, T. A. (1); Pavco, P. A. (1); Domenico, K. K. (1); Bellon, L. (1); Conrad, A. J.; Tong, M. J.; Blatt, L. M. (1)
CORPORATE SOURCE: (1) Ribozyme Pharm. Inc., Boulder, CO USA
SOURCE: Hepatology, (**Oct., 1998**) Vol. 28, No. 4 PART 2, pp. 398A.
Meeting Info.: Biennial Scientific Meeting of the International Association for the Study of the Liver and the 49th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases

Chicago, Illinois, USA November 4-10, 1998 International Association for the Study of the Liver
. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 17 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:48301 BIOSIS
DOCUMENT NUMBER: PREV199799347504
TITLE: **Hepatitis C virus**-specific hammerhead **ribozymes** cleave target RNA efficiently and inhibit viral gene expression.
AUTHOR(S): Alt, M.; Schuessler, S.; Steigerwald, R.; Hofschneider, P. H.; Caselmann, W. H.
CORPORATE SOURCE: Dep. Virus Research, Max-Planck-Inst. f. Biochemie, Martinsried Germany
SOURCE: Journal of Hepatology, (1996) Vol. 25, No. SUPPL. 1, pp. 73.
Meeting Info.: 31st Annual Meeting of the European Association for the Study of the Liver Geneva, Switzerland August 25-29, 1996
ISSN: 0168-8278.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L8 ANSWER 18 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:558573 BIOSIS
DOCUMENT NUMBER: PREV199699280929
TITLE: Comparison of three different hammerhead **ribozymes** for cleavage efficiency of **hepatitis C virus** RNA in vitro.
AUTHOR(S): Ohkawa, K.; Yuki, N.; Kanazawa, K.; Ueda, K.; Sasaki, Y.; Kasahara, A.; Hayashi, N.
CORPORATE SOURCE: First Dep. Med., Osaka Univ. Sch. Med., Suita, Osaka Japan
SOURCE: Hepatology, (1996) Vol. 24, No. 4 PART 2, pp. 396A.
Meeting Info.: 47th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Chicago, Illinois, USA November 8-12, 1996
ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 19 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:522910 BIOSIS
DOCUMENT NUMBER: PREV199598537210
TITLE: Inhibition of **hepatitis C virus** -directed translation by hammerhead **ribozymes** in vitro.
AUTHOR(S): Sakamoto, N.; Wu, C. H.; Wu, G. Y.
CORPORATE SOURCE: Dep. Med., Div. Gastroenterol.-Hepatol., Sch. Med., Univ. Conn. Health Cent., Farmington, CT USA
SOURCE: Hepatology, (1995) Vol. 22, No. 4 PART 2, pp. 330A.
Meeting Info.: 46th Annual Meeting and Postgraduate Course of the American Association for the Study of Liver Diseases Chicago, Illinois, USA November 3-7, 1995
ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 20 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 139:224402 CA
TITLE: Enzymatic nucleic acid treatment of diseases or

conditions related to hepatitis C virus infection
INVENTOR(S): Blatt, Lawrence; McSwiggen, James; Roberts, Elisabeth; Pavco, Pamela A.; MacJack, Dennis
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 172 pp., Cont.-in-part of U.S. Ser. No. 740,332. → mine
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 100
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003171311	A1	20030911	US 2001-817879	20010326
AU 9851819	A1	19980611	AU 1998-51819	19980112
AU 729657	B2	20010208		
US 2002082225	A1	20020627	US 1999-274553	19990323
AU 9939188	A1	19990916	AU 1999-39188	19990713
US 2002013458	A1	20020131	US 2000-504231	20000215
US 2003125270	A1	20030703	US 2000-740332	20001218

PRIORITY APPLN. INFO.:

US 1998-83217P	P	19980427
US 1998-100842P	P	19980918
US 1999-257608	B2	19990225
US 1999-274553	A2	19990323
US 2000-504231	A2	20000215
US 2000-611931	A2	20000707
US 2000-740332	A2	20001218
AU 1995-26422	A3	19950518
US 1996-623891	A	19960325

AB This invention relates to enzymic nucleic acid mols. (e.g., ribozymes and DNAzymes) directed to cleave RNA species of hepatitis C virus (HCV) and/or encoded by the HCV. Specifically, the present invention describes enzymic nucleic acid mols. that would cleave in the conserved regions of the HCV genome. In a preferred embodiment, the invention features the use of an enzymic nucleic acid mol., preferably in the hammerhead, Inozyme (NCH), G-cleaver, Amberzyme, Zinzyme and/or DNAzyme motif, to inhibit the expression and/or replication of HCV. Chem. modifications in the sugar, base, and/or phosphate backbones of these enzymic nucleic acids is carried out to improve their stability. Such enzymic nucleic acid mols. may be used to treat diseases assocd. with HCV infection. Ribozymes in combination with interferons and polyethylene glycol interferons which have the potential to improve the effectiveness of treatment of HCV are also described. [This abstr. record is one of two records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 21 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 139:79119 CA
TITLE: Enzymatic nucleic acid treatment of diseases or conditions related to hepatitis C virus infection
INVENTOR(S): Blatt, Lawrence; McSwiggen, James; Roberts, Elisabeth; Pavco, Pamela A.; Macejack, Dennis
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 198 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 100
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2003125270	A1	20030703	US 2000-740332	20001218	
AU 9851819	A1	19980611	AU 1998-51819	19980112	
AU 729657	B2	20010208			
AU 9939188	A1	19990916	AU 1999-39188	19990713	
US 2003125270	A1	20030703	US 2000-740332	20001218	
US 2003171311	A1	20030911	US 2001-817879	20010326	
US 2003171311	A1	20030911	US 2001-817879	20010326	

PRIORITY APPLN. INFO.:

AU 1995-26422	A3	19950518
US 1996-623891	A	19960325
US 1998-83217P	P	19980427
US 1998-100842P	P	19980918
US 1999-257608	B2	19990225
US 1999-274553	A2	19990323
US 2000-504231	A2	20000215
US 2000-611931	A2	20000707
US 2000-740332	A	20001218

AB This invention relates to enzymic nucleic acid mols. (e.g., ribozymes and DNAzymes) directed to cleave RNA species of hepatitis C virus (HCV) and/or encoded by the HCV. Specifically, the present invention describes enzymic nucleic acid mols. that would cleave in the conserved regions of the HCV genome. In a preferred embodiment, the invention features the use of an enzymic nucleic acid mol., preferably in the hammerhead, Inozyme (NCH), G-cleaver, amberzyme, zinzyme and/or DNAzyme motif, to inhibit the expression and/or replication of HCV. Chem. modifications in the sugar, base, and/or phosphate backbones of these enzymic nucleic acids is carried out to improve their stability. Such enzymic nucleic acid mols. may be used to treat diseases assocd. with HCV infection. Ribozymes in combination with interferons and polyethylene glycol interferons which have the potential to improve the effectiveness of treatment of HCV are also described. [This abstr. record is one of two records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 22 OF 55 CA COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 138:314544 CA

TITLE: Oligonucleotide-mediated inhibition of hepatitis B virus and hepatitis C virus replication

INVENTOR(S): Blatt, Lawrence; Macejak, Dennis; McSwiggen, James; Morrissey, David; Pavco, Pamela; Lee, Patrice; Draper, Kenneth; Roberts, Elisabeth

PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 387 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 100

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002081494	A1	20021017	WO 2002-XD9187	20020326
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, ML, MR, NE, SN, TD, TG				
AU 9851819	A1	19980611	AU 1998-51819	19980112

AU 729657	B2	20010208			
AU 9939188	A1	19990916	AU 1999-39188		19990713
US 2003171311	A1	20030911	US 2001-817879		20010326
US 2003068301	A1	20030410	US 2001-877478		20010608
US 2003148985	A1	20030807	US 2002-310294		20021205

PRIORITY APPLN. INFO.:

US 2001-817879	A	20010326
US 2001-296876P	P	20010608
US 2001-877478	A	20010608
US 2001-335059P	P	20011024
US 2001-337055P	P	20011205
US 1992-882712	B1	19920514
US 1994-193627	A1	19940207
AU 1995-26422	A3	19950518
US 1996-623891	A	19960325
US 1998-83217P	P	19980427
US 1998-100842P	P	19980918
US 1999-257608	B2	19990225
US 1999-274553	A2	19990323
US 1999-436430	A2	19991108
US 2000-504231	A2	20000215
US 2000-531025	A2	20000320
US 2000-611931	A2	20000707
US 2000-636385	A2	20000809
US 2000-696347	A2	20001024
US 2000-740332	A2	20001218

AB The present invention relates to nucleic acid mols., including antisense and enzymic nucleic acid mols., such as hammerhead ribozymes, DNAzymes, Inozymes, Zinzymes, Amberzymes, and G-cleaver ribozymes, which modulate the synthesis, expression and/or stability of a hepatitis C virus (HCV) or hepatitis B virus (HBV) RNA and methods for their use alone or in combination with other therapies. In addn., nucleic acid decoy mols. and aptamers that bind to HBV reverse transcriptase and/or HBV reverse transcriptase primer sequences and methods for their use alone or in combination with other therapies, are disclosed. Oligonucleotides that specifically bind the Enhancer I region of HBV DNA are further disclosed. The present invention further relates to the use of nucleic acids, such as decoy and aptamer mols. of the invention, to modulate the expression of HBV genes and HBV viral replication. Furthermore, HBV animal models and methods of use are disclosed, including methods of screening for compds. and/or potential therapies directed against HBV. The present invention also relates to compds., including enzymic nucleic acid mols., ribozymes, DNAzymes, nuclease-activating compds. and chimeras such as 2',5'-adenylates, that modulate the expression and/or replication of HCV. [This abstr. record is one of five records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 23 OF 55 CA COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	138:217448 CA
TITLE:	Synthesis of ribonucleic acids with RNase activity from modified nucleotide triphosphates and their ribozyme activity against hepatitis C virus and mammalian HER2 gene expression
INVENTOR(S):	Beigelman, Leonid; Burgin, Alex; Beaudry, Amber; Karpeisky, Alexander; Matulic-Adamic, Jasenka; Sweedler, David; Zinnen, Shawn
PATENT ASSIGNEE(S):	Ribozyme Pharmaceuticals, Incorporated, USA
SOURCE:	U.S., 70 pp., Cont.-in-part of U.S. Ser. No. 301,511. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	100

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6528640	B1	20030304	US 1999-474432	19991229
AU 9851819	A1	19980611	AU 1998-51819	19980112
AU 729657	B2	20010208		
EP 1321521	A1	20030625	EP 2003-2270	19980505
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 6127535	A	20001003	US 1998-186675	19981104
US 6482932	B1	20021119	US 1999-301511	19990428
AU 9939188	A1	19990916	AU 1999-39188	19990713
US 6617438	B1	20030909	US 1999-476387	19991230
US 6509460	B1	20030121	US 2000-644966	20000823
WO 2001016312	A2	20010308	WO 2000-US23998	20000830
WO 2001016312	A3	20010809		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1212416	A2	20020612	EP 2000-963298	20000830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2003004122	A1	20030102	US 2001-825805	20010404
US 2003105308	A1	20030605	US 2001-918728	20010731

PRIORITY APPLN. INFO.:

US 1997-64866P	P	19971105
US 1998-83727P	P	19980429
US 1998-186675	A2	19981104
US 1999-301511	A2	19990428
AU 1995-26422	A3	19950518
US 1996-623891	A	19960325
US 1997-46059P	P	19970509
US 1997-49002P	P	19970609
US 1997-51718P	P	19970703
US 1997-56808P	P	19970822
US 1997-61321P	P	19971002
US 1997-61324P	P	19971002
US 1997-68212P	P	19971219
EP 1998-920299	A3	19981112
US 1999-151713P	P	19990831
US 1999-156236P	P	19990927
US 1999-156467P	P	19990927
US 1999-406643	A	19990927
US 1999-436430	A	19991108
US 1999-169100P	P	19991206
US 1999-173612P	P	19991229
US 1999-474432	A2	19991229
US 1999-476387	A	19991230
US 2000-498824	A	20000204
US 2000-531025	A	20000320
US 2000-197769P	P	20000414
US 2000-578223	A	20000523
US 2000-636385	A	20000809
WO 2000-US23998	W	20000830
US 2001-825805	A2	20010404

AB Novel nucleotide triphosphates, methods of synthesis and process of incorporating these nucleotide triphosphates into oligonucleotides, and isolation of novel nucleic acid catalysts (e.g., ribozymes) are disclosed.

Also, described are the use of novel enzymic nucleic acid mols. (class I Amberzymes and class I Zinzymes) targeting hepatitis C virus RNA and to inhibit HER2/neu/c-erbB2 gene expression and their applications in human therapy.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 55 CA COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 138:78419 CA

TITLE: Method of inhibiting HER2 expression and treating cancer with chemotherapeutic agent-ribozyme/DNAzyme combination

INVENTOR(S): Beigelman, Leonid; Burgin, Alex; Beaudry, Amber; Karpeisky, Alexander; Matulic-Adamic, Jasenka; Sweedler, David; Zinnen, Shawn

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 105 pp., Cont.-in-part of U.S. Ser. No. 578,223.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 100

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 2003004122	A1	20030102	US 2001-825805	20010404	
AU 9851819	A1	19980611	AU 1998-51819	19980112	<--
AU 729657	B2	20010208			
EP 1321521	A1	20030625	EP 2003-2270	19980505	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY					
US 6127535	A	20001003	US 1998-186675	19981104	<--
US 6482932	B1	20021119	US 1999-301511	19990428	
AU 9939188	A1	19990916	AU 1999-39188	19990713	<--
US 6528640	B1	20030304	US 1999-474432	19991229	
US 6617438	B1	20030909	US 1999-476387	19991230	
US 6509460	B1	20030121	US 2000-644966	20000823	
US 2003105308	A1	20030605	US 2001-918728	20010731	

PRIORITY APPLN. INFO.:

US 1997-64866P	P	19971105
US 1998-83727P	P	19980429
US 1998-186675	A2	19981104
US 1999-301511	A2	19990428
US 1999-474432	A2	19991229
US 1999-476387	A2	19991230
US 2000-578223	A2	20000523
AU 1995-26422	A3	19950518
US 1996-623891	A	19960325
US 1997-46059P	P	19970509
US 1997-49002P	P	19970609
US 1997-51718P	P	19970703
US 1997-56808P	P	19970822
US 1997-61321P	P	19971002
US 1997-61324P	P	19971002
US 1997-68212P	P	19971219
EP 1998-920299	A3	19981112
US 2001-825805	A2	20010404

AB The present invention relates to nucleic acid catalysts (e.g., ribozymes or DNAzymes) and their use for inhibition of HER2/neu/ErbB2 gene expression and for cancer therapy. Thus, ribozymes consisting primarily of 2'-O-methylribosides and contg. phosphorothioate-linked 5'-terminal residues and an inverted deoxyabasic residue as well as

2'-deoxy-2'-aminocytidine were prepd. These ribozymes inhibited HER2 gene expression in SK-BR-3 and SK-OV-3 cells. An additive effect was obsd. when the ribozymes were admininistered with chemotherapeutic agents paclitaxel, doxorubicin, and cisplatin.

L8 ANSWER 25 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 137:381696 CA
TITLE: Hepatitis C virus-cleaving catalytic nucleic acids and their therapeutic use
INVENTOR(S): Beigelman, Leonid; Burgin, Alex; Beaudry, Amber; Karpeisky, Alexander; Matulic-Adamic, Jasenka; Sweedler, David; Zinnen, Shawn
PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Incorporated, USA
SOURCE: U.S., 67 pp., Cont.-in-part of U.S. 6,127,535.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 100
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 6482932	B1	20021119	US 1999-301511	19990428	
AU 9851819	A1	19980611	AU 1998-51819	19980112	<--
AU 729657	B2	20010208			
EP 1321521	A1	20030625	EP 2003-2270	19980505	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY					
US 6127535	A	20001003	US 1998-186675	19981104	<--
AU 9939188	A1	19990916	AU 1999-39188	19990713	<--
US 6528640	B1	20030304	US 1999-474432	19991229	
US 6617438	B1	20030909	US 1999-476387	19991230	
US 6509460	B1	20030121	US 2000-644966	20000823	
US 2003004122	A1	20030102	US 2001-825805	20010404	
US 2003105308	A1	20030605	US 2001-918728	20010731	

PRIORITY APPLN. INFO.:

US 1997-64866P	P	19971105
US 1998-83727P	P	19980429
US 1998-186675	A2	19981104
AU 1995-26422	A3	19950518
US 1996-623891	A	19960325
US 1997-46059P	P	19970509
US 1997-49002P	P	19970609
US 1997-51718P	P	19970703
US 1997-56808P	P	19970822
US 1997-61321P	P	19971002
US 1997-61324P	P	19971002
US 1997-68212P	P	19971219
EP 1998-920299	A3	19981112
US 1999-301511	A2	19990428
US 1999-474432	A2	19991229
US 1999-476387	A2	19991230
US 2000-578223	A2	20000523
US 2001-825805	A2	20010404

AB Catalytic nucleic acids (**ribozymes**, DNAzymes) which cleave **hepatitis C virus** RNA are disclosed. These catalytic nucleic acids may contain altered internucleoside linkages (e.g., amide, phosphorothioate, phosphorodithioate) as well as 2'-modified nucleosides such as 2'-O-aminocytidine or 2'-deoxy-2'-aminocytidine. The ribozymes/DNAzymes may be used to inhibit expression of hepatitis C virus genes.

REFERENCE COUNT: 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L8 ANSWER 26 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 136:354491 CA
TITLE: Nucleic acid-based ribozyme and DNAzyme modulators of gene expression
INVENTOR(S): McSwiggen, James; Usman, Nassim; Blatt, Lawrence; Beigelman, Leonid; Burgin, Alex; Karpeisky, Alexander; Matulic-Adamic, Jasenka; Sweedler, David; Draper, Kenneth; Chowrira, Bharat; Stinchcomb, Dan; Beaudry, Amber; Zinnen, Shawn; Lugwig, Janos; Sproat, Brian S.
PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 717 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 100
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016312	A2	20010308	WO 2000-US23998	20000830
WO 2001016312	A3	20010809		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9851819	A1	19980611	AU 1998-51819	19980112
AU 729657	B2	20010208		
AU 9939188	A1	19990916	AU 1999-39188	19990713
US 6528640	B1	20030304	US 1999-474432	19991229
US 6617438	B1	20030909	US 1999-476387	19991230
EP 1212416	A2	20020612	EP 2000-963298	20000830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2003050259	A1	20030313	US 2000-730289	20001205

PRIORITY APPLN. INFO.:

US 1999-151713P	P	19990831
US 1999-156236P	P	19990927
US 1999-156467P	P	19990927
US 1999-406643	A	19990927
US 1999-436430	A	19991108
US 1999-169100P	P	19991206
US 1999-173612P	P	19991229
US 1999-474432	A	19991229
US 1999-476387	A	19991230
US 2000-498824	A	20000204
US 2000-531025	A	20000320
US 2000-197769P	P	20000414
US 2000-578223	A	20000523
US 2000-636385	A	20000809
AU 1995-26422	A3	19950518
US 1996-623891	A	19960325
US 1997-64866P	P	19971105
US 1998-83727P	P	19980429
US 1998-186675	A2	19981104
US 1999-301511	A2	19990428
WO 2000-US23998	W	20000830

AB Novel nucleic acid mols. useful as inhibitors of gene expression, compns., and methods for their use are provided. The invention features novel

nucleic acid-based techniques (e.g., enzymic nucleic acid mols. (ribozymes), antisense nucleic acids, 2-5A antisense chimeras, triplex DNA, and antisense nucleic acids contg. RNA-cleaving chem. groups) and their use to modulate the expression of mol. targets impacting the development and progression of cancers, diabetes, obesity, Alzheimer's disease diseases, age-related diseases, and/or hepatitis B infections and related conditions. Catalytic nucleic acids were designed for site-specific cleavage of human mRNA targets encoding protein tyrosine phosphatase 1b, methionine aminopeptidase, .beta.-secretase, presenilin-1, epidermal growth factor receptor-2 (HER2/c-erb2/neu), phospholamban, telomerase, and hepatitis B virus genes. Methods for chem. synthesis of modified nucleoside triphosphates (NTPs) and RNA polymerase-catalyzed incorporation of modified NTPs into catalytic oligonucleotides are also provided. [This abstr. record is one of 6 records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 27 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 136:145203 CA
TITLE: Ribozymes for treatment of diseases or conditions related to hepatitis C virus infection
INVENTOR(S): Blatt, Lawrence; McSwiggen, James A.; Roberts, Elisabeth; Pavo, Pamela A.; Macejack, Dennis
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 65 pp., Cont.-in-part of U.S. Ser. No. 274,553.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 100
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 2002013458	A1	20020131	US 2000-504231	20000215	
AU 9851819	A1	19980611	AU 1998-51819	19980112	<--
AU 729657	B2	20010208			
US 2002082225	A1	20020627	US 1999-274553	19990323	
AU 9939188	A1	19990916	AU 1999-39188	19990713	<--
US 2003171311	A1	20030911	US 2001-817879	20010326	
US 2003171311	A1	20030911	US 2001-817879	20010326	

PRIORITY APPLN. INFO.:

US 1999-274553	A2	19990323
AU 1995-26422	A3	19950518
US 1996-623891	A	19960325
US 1998-83217P	P	19980427
US 1998-100842P	P	19980918
US 1999-257608	B2	19990225
US 2000-504231	A2	20000215
US 2000-611931	A2	20000707
US 2000-740332	A2	20001218

AB Ribozymes that inhibit gene expression or RNA replication by hepatitis C virus (hc bpV) are described for use in the treatment of infection. Potential cleavage sites were identified by screening for unstructured regions of the viral RNA. Candidate ribozymes were tested for their ability to inhibit expression of the downstream reporter gene in a dicistronic luciferase expression system.

L8 ANSWER 28 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 135:353653 CA
TITLE: Intracellular incision activity of **Ribozyme** specific to **hepatitis C virus**

AUTHOR(S): Yang, Jianyang; Hong, Shiwen; Mao, Pannan; Liang, Yong; Ju, Liancai; Hu, Yan
CORPORATE SOURCE: Department of Virus, No.302 Hospital of PLA, Beijing, 100039, Peop. Rep. China
SOURCE: Zhongguo Gonggong Weisheng (**2000**), 16(5), 400-401
CODEN: ZGWEE3; ISSN: 1001-0580
PUBLISHER: Zhongguo Gonggong Weisheng Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB One Ribozyme Rz386 was designed and synthesized based on HCV core gene (384-386nt). The incision activity Ribozyme Rz386 was detd. by extg. HCV RNA from serum of patient with HCV, amplifying to obtain 412 bp HCV DNA; cloning resp. Rz386 gene and HCV DNA into transcriptional vector pLXN to obtain recombinant plasmids pLXN-Rz386 and pLXN-HCV; transferring resp. into packaging cell PA317; co-transfecting blank cell PA317; culturing, and detecting by RT-PCR. There was no HCV in culture liquor of blank cell PA317. The results showed that Ribozyme had the activity of intracellularly incising HCV RNA.

L8 ANSWER 29 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 133:307013 CA
TITLE: Quantitative Determination of a Chemically Modified Hammerhead Ribozyme in Blood Plasma Using 96-Well Solid-Phase Extraction Coupled with High-Performance Liquid Chromatography or Capillary Gel Electrophoresis
AUTHOR(S): Bellon, Laurent; Maloney, Lara; Zinnen, Shawn P.; Sandberg, Jennifer A.; Johnson, Kevin E.
CORPORATE SOURCE: Department of Oligonucleotide Chemistry, Ribozyme Pharmaceuticals, Inc., Boulder, CO, 80301, USA
SOURCE: Analytical Biochemistry (**2000**), 283(2), 228-240
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Versatile bioanal. assays to detect chem. stabilized hammerhead ribozyme and putative ribozyme metabolites from plasma are described. The extn. protocols presented are based on serial solid-phase extns. performed on a 96-well plate format and are compatible with either IEX-HPLC or CGE back-end anal. A validation of both assays confirmed that both the HPLC and the CGE methods possess the required linearity, accuracy, and precision to accurately measure concns. of hammerhead ribozyme extd. from plasma. These methods should be of general use to detect and quantitate ribozymes from other biol. fluids such as serum and urine. (c) 2000 Academic Press.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 133:276316 CA
TITLE: Hepatitis C virus cell culture system for development and evaluation of antiviral agents
INVENTOR(S): Bartenschlager, Ralf
PATENT ASSIGNEE(S): Johannes-Gutenberg-Universitaet Mainz, Germany
SOURCE: Ger. Offen., 58 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19915178	A1	20001005	DE 1999-19915178	19990403 <--
EP 1043399	A2	20001011	EP 2000-105929	20000323 <--
EP 1043399	A3	20020508		
EP 1043399	B1	20030409		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 236988	E	20030415	AT 2000-105929	20000323
CA 2303526	AA	20001003	CA 2000-2303526	20000331 <--
JP 2001017187	A2	20010123	JP 2000-101615	20000403

PRIORITY APPLN. INFO.: DE 1999-19915178 A 19990403

AB The title cell culture system comprises a human hepatoma cell contg. an hepatitis C virus (HCV) RNA construct. The HCV construct contains, in addn. to a selectable marker gene, the following HCV elements/genes: 5'NTR, NS3, NS4A, NS4B, NS5A, NS5B, and 3'NTR. This cell culture system provides for the first time an in vitro system in which HCV RNA is replicated autonomously and in large enough quantities that conventional biochem. methods can be used to quantitate it as well as the proteins produced from the RNA. The system may be used to screen for or evaluate potential antiviral agents.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 31 OF 55 CA COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 133:145575 CA

TITLE: Intracellular immunization by hammerhead **ribozyme** against **hepatitis C virus**

AUTHOR(S): Zhou, Yongxing; Jia, Zhansheng; Lian, Jianqi; Feng, Zhihua; Jiao, Chengsong; Li, Jinge

CORPORATE SOURCE: Department of Infectious Diseases, Tangdu Hospital, Fourth Military Medical University, Xi'an, 710038, Peop. Rep. China

SOURCE: Disi Junyi Daxue Xuebao (**2000**), 21(7), 796-798
CODEN: DJDXEG; ISSN: 1000-2790

PUBLISHER: Disi Junyi Daxue Xuebao Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The protective effect of hammerhead **ribozymes** (Rz213) against **hepatitis C virus** (HCV) from viral gene transfection was studied. Rz213 cleaving 5' noncoding region (5' NCR) of HCV line was beforehand transfected in a human hepatic carcinoma cell (HHCC) and selected for G418 resistance. Cells stably expressing Rz213 were retransfected by pCMVNCRluc contg. 5' NCR-luc fusion genes by LipofectAMINE, and then the luciferase activity in the lysis was measured by scintillation counting. HHCC cells stably expressing Rz213 showed significant resistance to retransfection of targeting gene. The results showed that the ribozymes-213 against HCV 5' NCR could be substantially and specifically expressed in HHCC, and the expression may cause an intracellular immunization.

L8 ANSWER 32 OF 55 CA COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 133:86096 CA

TITLE: Enhancement of ribozyme catalytic activity with 2'-O-substituted facilitator oligonucleotide

INVENTOR(S): Goodchild, John

PATENT ASSIGNEE(S): University of Massachusetts Worcester, USA

SOURCE: U.S., 15 pp., 5612469 Cont.-in-part of U.S. 5,612,469.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6087484	A	20000711	US 1997-819942	19970318 <--
US 5612469	A	19970318	US 1995-431625	19950501 <--

PRIORITY APPLN. INFO.: US 1992-830713 B1 19920204
US 1993-138896 B1 19931019
US 1995-431625 A2 19950501

AB Methods are disclosed for increasing ribozyme catalytic activity without reducing specificity, which methods comprise contacting an RNA mol. with a ribozyme and a 2'-O-substituted facilitator oligonucleotide. The facilitator oligonucleotide binds to the substrate RNA at a site contiguous to the ribozyme binding site. The present invention further provides compns. comprising a ribozyme and an effective amt. of a 2'-O-Me substituted facilitator oligonucleotide. The use of a facilitator, particularly a 2'-O-substituted facilitator, and more esp. a 2'-O-Me substituted facilitator, greatly enhances ribozyme catalytic activity, frequently making an otherwise inactive ribozyme active. The method was demonstrated with **ribozymes** targeted to HIV-1 and **hepatitis C virus** RNAs as well as to VEGF mRNA. Both length and presence/absence of 2'-O-Me groups in the oligoribonucleotide facilitator affected the efficiency of substrate cleavage.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 33 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 132:246338 CA
TITLE: **Ribozymes** cleaving **hepatitis C virus** RNA and their use in the treatment of infection
INVENTOR(S): Barber, Jack R.; Welch, Peter J.; Tritz, Richard; Yei, Soonpin; Yu, Mang
PATENT ASSIGNEE(S): Immusol Inc., USA
SOURCE: U.S., 57 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6043077	A	20000328	US 1997-954210	19971020 <--
US 6458567	B1	20021001	US 1999-431419	19991101

PRIORITY APPLN. INFO.: US 1996-608862 B2 19960229
US 1997-954210 A1 19971020

AB Ribozymes useful in the treatment or prophylaxis of hepatitis C virus (HCV) infection or disease are described. The ribozyme may be delivered to a subject using an expression vector to manuf. the ribozyme in vivo. Alternatively, the ribozyme may be delivered ex vivo or in vitro. Ribozymes active against the (+) and (-) strands of the viral RNA are described. The use of an adenovirus vector to deliver a ribozyme gene to Huh7 cells with synthesis of the ribozyme is demonstrated.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 34 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 132:218868 CA

TITLE: Methods of preparation of prodrug **ribozymes** for inhibiting **hepatitis C virus**
INVENTOR(S): Tohdoh, Naoki; Yamamoto, Hiroko; Sudo, Yoshiaki
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000014252	A1	20000316	WO 1999-JP4767	19990902 <--
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1111057	A1	20010627	EP 1999-940630	19990902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: JP 1998-249900 A 19980903
WO 1999-JP4767 W 19990902

AB A gene encoding a prodrug ribozyme which can be converted into a functional ribozyme in the cytoplasm after splicing is described. The prodrug ribozyme, which has no RNA-cleaving activity, contains an intervening sequence that can be eliminated by splicing. Prepn. of a prodrug ribozyme targeting the (+) or (-) strand of NS5B (RNA-dependent RNA polymerase) region of **hepatitis C virus** (HCV), and use of the **ribozymes** as HCV inhibitors are demonstrated.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 35 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 131:346489 CA
TITLE: Enzymatic nucleic acid treatment of diseases or conditions related to hepatitis c virus infection
INVENTOR(S): Blatt, Lawrence; Mcswiggen, James A.; Roberts, Elisabeth; Pavco, Pamela A.; Macejak, Dennis
PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 100
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955847	A2	19991104	WO 1999-US9027	19990426
WO 9955847	A3	20000615		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9851819	A1	19980611	AU 1998-51819	19980112

AU 729657	B2	20010208				
US 2002082225	A1	20020627	US 1999-274553		19990323	
CA 2326695	AA	19991104	CA 1999-2326695		19990426	
AU 9936657	A1	19991116	AU 1999-36657		19990426	
AU 757034	B2	20030130				
EP 1075508	A2	20010214	EP 1999-918837		19990426	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI						
AU 9939188	A1	19990916	AU 1999-39188		19990713	
PRIORITY APPLN. INFO.:			US 1998-83217P	P	19980427	
			US 1998-100842P	P	19980918	
			US 1999-257608	A	19990225	
			US 1999-274553	A	19990323	
			AU 1995-26422	A3	19950518	
			US 1996-623891	A	19960325	
			WO 1999-US9027	W	19990426	

AB Enzymic nucleic acid mols. which modulate the expression and/or replication of hepatitis C are disclosed. Ribozymes capable of in vitro and in vivo cleavage of hepatitis C virus RNA are prepd. and tested.

L8 ANSWER 36 OF 55 CA COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 131:334122 CA

TITLE: Modified nucleoside triphosphates and their synthesis and incorporation into gene expression-inhibiting ribozymes

INVENTOR(S): Beigelman, Leonid; Burgin, Alex; Beaudry, Amber; Karpeisky, Alexander; Matulic-Adamic, Jasenka; Sweedler, David; Zinnen, Shawn

PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 100

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9955857	A2	19991104	WO 1999-US9348		19990428	<--
WO 9955857	A3	20000224				
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG						
AU 9851819	A1	19980611	AU 1998-51819		19980112	<--
AU 729657	B2	20010208				
US 6127535	A	20001003	US 1998-186675		19981104	<--
CA 2330574	AA	19991104	CA 1999-2330574		19990428	<--
AU 9938724	A1	19991116	AU 1999-38724		19990428	<--
AU 751480	B2	20020815				
EP 1073732	A2	20010207	EP 1999-921537		19990428	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI						
JP 2002512794	T2	20020508	JP 2000-546001		19990428	
AU 9939188	A1	19990916	AU 1999-39188		19990713	<--
PRIORITY APPLN. INFO.:			US 1998-83727P	P	19980429	
			US 1998-186675	A	19981104	
			AU 1995-26422	A3	19950518	

	US 1996-623891	A	19960325
	US 1997-64866P	P	19971105
	WO 1999-US9348	W	19990428

OTHER SOURCE(S): MARPAT 131:334122

AB Novel nucleotide triphosphates, methods of synthesis and process of incorporating these nucleotide triphosphates into oligonucleotides, and isolation of novel nucleic acid catalysts (e.g., ribozymes) are disclosed. Thus, a process for synthesizing pyrimidine triphosphates comprises monophosphorylation using a phosphorylating agent (e.g. POCl3) and trialkyl phosphate (such as tri-Et phosphate) in the presence of dimethylaminopyridine (DMAP). The presence of DMAP increases the yield and decreases the reaction time. The pyrimidine monophosphate is then contacted with a pyrophosphorylating agent such as tributylammonium pyrophosphate to prep. the triphosphate. The incorporation of modified nucleosides such as 2'-deoxy-2'-aminocytidine into ribozymes using RNA polymerase can be increased by the presence of LiCl, MeOH, PEG, PrOH, EtOH, CH3NH2, or Et2O in the reaction mixt. A novel ribozyme contg. 2'-deoxy-2'-aminocytidine and 2'-deoxy-2'-aminouridine which cleaved hepatitis C virus RNA in vivo with IC50 of 5 nM was prepd.

L8 ANSWER 37 OF 55 CA COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 131:83948 CA

TITLE: Computerized design of **hepatitis C virus** RNA-directed hammerhead **ribozymes**

AUTHOR(S): Jia, Zhan-Sheng; Zhou, Yong-Xing; Lian, Jian-Qi; Feng, Zhi-Hua; Li, Guang-Yu; Zhang, Wen-Bin

CORPORATE SOURCE: Tangdu Infectious Diseases Hospital, Fourth Military Medical University, Xi'an, 710038, Peop. Rep. China

SOURCE: Shijie Huaren Xiaohua Zazhi (**1999**), 7(4), 300-302
CODEN: SHXZF2

PUBLISHER: Shijie Weichangbingxue Zazhishe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB To design the hammerhead multi-unit ribozymes (RZ) which may specifically cleave 5' noncoding region (5'NCR) and core region of hepatitis C virus (HCV) RNA. The possible secondary structures of RNA sequence of HCV-H (1a) strain which was taken as the targeting RNA was predicted, the ideal cleavage sites were selected, and their ribozymes were designed with computer according to the principle of the "hammerhead structure" RZ and the lowest energy. And then the sequence (7 - 8 nt) around the cleavage sites was compared with other 4 HCV strains. The four sites 213 (CUC), 260 (GUA), 407 (GUC) and 498 (CUU) were selected from the 124 natural sites (CUX and GUX) in 5' NCR and C region of HCV-H RNA. The sequences (7 - 8 nt) around the four sites which could be bound by their ribozymes were homogeneous among 5 HCV strains. Computer may be used as a helpful aid for designing the ribozymes against various virus RNA or mRNA. The 213, 260, 407 and 498 in 5' NCR and C region of HCV RNA may be the most ideal cleavage sites.

L8 ANSWER 38 OF 55 CA COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 130:134582 CA

TITLE: Cleavage of **hepatitis C virus** RNA by specific **ribozymes**

AUTHOR(S): Liu, Li-zhong; Wang, Sheng-qi; Zhu, Bao-zhen; Sun, Zhi-xian

CORPORATE SOURCE: Beijing Institute Radiation Medicine, Beijing, 100850, Peop. Rep. China

SOURCE: Shengwu Huaxue Yu Shengwu Wuli Jinzhan (**1998**), 25(5), 449-453
CODEN: SHYCD4; ISSN: 1000-3282

PUBLISHER: Shengwu Huaxue Yu Shengwu Wuli Jinzhan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Four kinds of different hammerhead ribozymes (ribozyme A, ribozyme B, ribozyme C1, ribozyme C2) were designed and synthesized according to the secondary structure of hepatitis C virus (HCV) RNA 5'-untranslated region and part of the neighbor C-region. And ribozyme RzA was able to cut at the GTA.dwnarw. motif at the -11 nt site of HCV-RNA. RzA-RNA and the combinated pC1-neo-luciferase in which a luciferase gene were ligated downstream the target sequence were then co-transfected into HepG2 cell lines with lipofectin. The cleavage of RzA-RNA was tested by detd. the expression of luciferase gene. Therefore, the gene of RzA was ligated into expression vector pC1-neo. The pC1-neo-RzA plamid and the vector pC1-neo-luciferase were co-transfected into HepG2 cell lines again with lipofectin. Since the pC1-neo-RzA was more stable than RzA-RNA in vivo and could produce RzA-RNA continuously, it showed better cleavage activity.

L8 ANSWER 39 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 130:92125 CA
TITLE: Hammerhead ribozymes with extended cleavage specificity
INVENTOR(S): Ludwig, Janos; Sproat, Brian S.
PATENT ASSIGNEE(S): Innovir Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9858058	A1	19981223	WO 1998-US12663	19980617	<--
W: AU, CA, JP					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9879761	A1	19990104	AU 1998-79761	19980617	<--
EP 1019497	A1	20000719	EP 1998-930352	19980617	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002510207	T2	20020402	JP 1999-504776	19980617	

PRIORITY APPLN. INFO.: US 1997-878640 A 19970619
WO 1998-US12663 W 19980617

OTHER SOURCE(S): MARPAT 130:92125
AB Disclosed are compns. having an RNA-cleavage activity, as well as their use for cleaving RNA-substrates in vitro and in vivo. The compns. contain an active center, the subunits of which are selected from nucleotides and/or nucleotide analogs, as well as flanking regions contributing to the formation of a specific hybridization with an RNA substrate. Preferred compns. form, in combination with an RNA substrate, a structure resembling a hammerhead structure. Gerlach-type ribozyme analogs contg. an inosine at position 15.1 (numbered according to the std. nomenclature of Hertel et al. (1992)) readily cleave RNA substrates contg. an N16.2C16.1H17 triplet. It is preferred that H17 is not guanosine. The ability to cleave substrates having N16.2C16.1H17 triplets effectively doubles the no. of targets available for cleavage by compns. of the type disclosed. Catalytic **ribozymes** are designed for cleave of **hepatitis C virus** RNA, human interleukin-2 mRNA, rat dopamine D2 receptor mRNA, and human ICAM-1 mRNA.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 40 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 128:189185 CA
TITLE: Galactosyltransferase-comprising baculovirus expression system for hepatocyte-targeted gene expression and treatment of liver diseases
INVENTOR(S): Jarvis, Donald L.; Lanford, Robert
PATENT ASSIGNEE(S): Texas A & M University System, USA; Southwest Foundation for Biomedical Research; Jarvis, Donald L.; Lanford, Robert
SOURCE: PCT Int. Appl., 247 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9806855	A1	19980219	WO 1997-US14504	19970815 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9742318	A1	19980306	AU 1997-42318	19970815 <--

PRIORITY APPLN. INFO.: US 1996-24078P P 19960816
WO 1997-US14504 W 19970815

AB Disclosed are recombinant baculoviruses that are used to deliver hepatocyte-expressible nucleic acid constructs specifically to hepatocytes. Also provided are a variety of recombinant baculovirus vectors which comprise at least one oligosaccharide-processing enzyme gene and a hepatocyte-expressible nucleic acid segment. The invention also provides methods of using the expression systems and recombinant baculoviruses, particularly in the treatment of liver diseases and/or infections. Thus, baculovirus expressing bovine .beta.-1,4-galactosyltransferase from the baculovirus ie1 promoter and hr5 enhancer produced virions contg. galactosylated gp64. This modification of the virion glycoprotein is expected to facilitate its interaction with hepatocytes and to allow delivery of therapeutic nucleic acids to hepatocytes at low multiplicities of infection.

REFERENCE COUNT: 374 THERE ARE 374 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 41 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 128:111543 CA
TITLE: Enzymic preparation of ribozyme library or antisense RNA library in absence of templates and primers
INVENTOR(S): Miura, Takanori; Ogata, Norio
PATENT ASSIGNEE(S): Taiko Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 10004964	A2	19980113	JP 1996-162607	19960624 <--
JP 3291554	B2	20020610		

PRIORITY APPLN. INFO.: JP 1996-162607 19960624

AB Prepn. of templates- and primers-independent RNA assembly (NT-RNA) by using thermostable DNA polymerase from Thermococcus or Thermus is described. The method is useful for the prepn. of a ribozyme library or an antisense RNA library that can respond to the polymorphism of viral RNA. Prepn. of a RNA assembly using thermostable RNA polymerase from Thermococcus litoralis or Thermus thermophilus, and assessment of the ribozyme activities of the RT-RNA to the RNA of HIV-1, HIV-2, and HCV (hepatitis C virus) were demonstrated.

L8 ANSWER 42 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 127:243249 CA
TITLE: **Ribozymes** cleaving **hepatitis C virus** RNA and their use in the treatment of infection
INVENTOR(S): Barber, Jack R.; Welch, Peter J.; Tritz, Richard; Yei, Soonpei; Yu, Mang
PATENT ASSIGNEE(S): Immusol, Inc., USA; Barber, Jack R.; Welch, Peter J.; Tritz, Richard; Yei, Soonpei; Yu, Mang
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732018	A2	19970904	WO 1997-US3304	19970227 <--
WO 9732018	A3	19971009		
W: AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9720642	A1	19970916	AU 1997-20642	19970227 <--
EP 914421	A2	19990512	EP 1997-908831	19970227 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000506010	T2	20000523	JP 1997-531197	19970227 <--

PRIORITY APPLN. INFO.: US 1996-608862 A 19960229
WO 1997-US3304 W 19970227

AB Ribozymes useful in the treatment or prophylaxis of Hepatitis C Virus (HCV) infection or disease are described. The ribozyme may be delivered to a subject using an expression vector to manuf. the ribozyme in vivo. Alternatively, the ribozyme may be delivered ex vivo or in vitro. Ribozymes active against the (+) and (-) strands of the viral RNA are described. The use of an adenovirus vector to deliver a ribozyme gene to Huh7 cells with synthesis of the ribozyme is demonstrated.

L8 ANSWER 43 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 126:260123 CA
TITLE: Enzymic RNA molecule targeted against Hepatitis C virus
INVENTOR(S): Draper, Kenneth G.
PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc., USA

SOURCE: U.S., 96 pp., Cont.-in-part of U.S. Ser.No. 882,888, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 100
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 5610054	A	19970311	US 1994-182968	19940113	<--
CA 2180740	AA	19950720	CA 1995-2180740	19950112	<--
WO 9519429	A2	19950720	WO 1995-US495	19950112	<--
WO 9519429	A3	19950908			
W: AU, CA, JP, KR, MX					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9515665	A1	19950801	AU 1995-15665	19950112	<--
EP 737247	A1	19961016	EP 1995-907430	19950112	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 09508018	T2	19970819	JP 1995-519142	19950112	<--
US 5869253	A	19990209	US 1996-774306	19961226	<--
AU 9851819	A1	19980611	AU 1998-51819	19980112	<--
AU 729657	B2	20010208			
US 6132966	A	20001017	US 1998-64156	19980421	<--
AU 9939188	A1	19990916	AU 1999-39188	19990713	<--

PRIORITY APPLN. INFO.:

US 1992-882888	B2	19920514
US 1994-182968	A	19940113
WO 1995-US495	W	19950112
AU 1995-26422	A3	19950518
US 1996-623891	A	19960325
US 1996-774306	A1	19961223

AB Disclosed are 506 enzymic RNA mol. which specifically cleaves RNA of a hepatitis C virus.

L8 ANSWER 44 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 126:248757 CA
TITLE: Novel 3' terminal sequences of hepatitis C virus RNA and their use in the generation of infectious virus for diagnostic and therapeutic use
INVENTOR(S): Rice, Charles Iii; Kolykhalov, Alexander A.
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9708310	A1	19970306	WO 1996-US14033	19960828	<--
W: AL, AU, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
US 5874565	A	19990223	US 1995-520678	19950829	<--
CA 2230452	AA	19970306	CA 1996-2230452	19960828	<--
AU 9669097	A1	19970319	AU 1996-69097	19960828	<--
AU 713112	B2	19991125			
EP 856051	A1	19980805	EP 1996-929843	19960828	<--

EP 856051	B1	20020403			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
BR 9610307	A	19990706	BR 1996-10307	19960828	<--
JP 11514241	T2	19991207	JP 1997-510618	19960828	<--
ES 2174097	T3	20021101	ES 1996-929843	19960828	
US 6297003	B1	20011002	US 1997-897126	19970718	
US 2003017586	A1	20030123	US 2001-880567	20010613	
US 2003027130	A1	20030206	US 2001-880508	20010613	
US 2003054341	A1	20030320	US 2002-158314	20020530	

PRIORITY APPLN. INFO.: US 1995-520678 A 19950829
WO 1996-US14033 W 19960828
US 1997-897126 A1 19970718
US 1999-368958 A1 19990805

AB Novel RNA sequences found at the 3' terminus of hepatitis C virus (HCV) RNA are characterized for diagnostic and therapeutic use. These sequences are strongly conserved amongst isolates and so are useful for nucleic-acid based diagnostics and for developing and evaluating novel anti-HCV therapies. This sequence element is likely to be essential for viral replication, and required for construction of full-length HCV cDNA clones capable of yielding infectious RNA, progeny virus or replication-competent HCV replicons. Such functional clones are useful tools for evaluation of therapeutic approaches and as substrates for developing candidate attenuated or inactivated HCV derivs. for vaccination against HCV. These 3' sequences form a stable hairpin loop that is essential for viral replication. The homopolymer tract that was believed to be the 3'-terminus of the virus is note essential for replication.

L8 ANSWER 45 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 126:45740 CA
TITLE: Elimination of hepatitis C virus RNA in infected human hepatocytes by adenovirus-mediated expression of ribozymes
AUTHOR(S): Lieber, Andre; He, Cheng-Yi; Polyak, Stephen J.; Gretch, David R.; Barr, Darlene; Kay, Mark A.
CORPORATE SOURCE: Div. Med. Genet., Univ. Washington, Seattle, WA, USA
SOURCE: Journal of Virology (**1996**), 70(12), 8782-8791
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hepatitis C virus (HCV), a pos.-strand RNA virus, is the major infectious agent responsible for causing chronic hepatitis. Currently, there is no vaccine for HCV infection, and the only therapy for chronic hepatitis C is largely ineffective. To investigate new genetic approaches to the management of HCV infection, six hammerhead ribozymes directed against a conserved region of the plus strand and minus strand of the HCV genome were isolated from a ribozyme library, characterized, and expressed from recombinant adenovirus vectors. The expressed ribozymes individually or in combination were efficient at reducing or eliminating the resp. plus- or minus-strand HCV RNAs expressed in cultured cells and from primary human hepatocytes obtained from chronic HCV-infected patients. This study demonstrates the potential utility of ribozyme therapy as a strategy for the treatment of hepatitis C virus infection.

L8 ANSWER 46 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 125:105168 CA
TITLE: Recombinant vectors for permanent reconstitution of liver and treatment of hepatitis C
INVENTOR(S): Kay, Mark A.; Lieber, Andre
PATENT ASSIGNEE(S): University of Washington, USA

SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9618419	A1	19960620	WO 1995-US16347	19951214 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6107027	A	20000822	US 1995-534220	19950911 <--
AU 9645198	A1	19960703	AU 1996-45198	19951214 <--
EP 797455	A1	19971001	EP 1995-943818	19951214 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10510815	T2	19981020	JP 1995-519274	19951214 <--

PRIORITY APPLN. INFO.:
US 1994-357508 A 19941214
US 1995-476257 A 19950607
US 1995-534220 A 19950911
WO 1995-US16347 W 19951214

AB A combination of retroviral and adenoviral vectors are used for high efficiency gene transfer into hepatocytes, resulting in long term gene expression. Hepatocytes are transduced in vitro with a recombinant adenovirus vector that expresses a mol. capable of inducing hepatocyte regeneration, such as urokinase plasminogen activator (uPA) or tissue plasminogen activator (tPA), resulting in a high rate of liver regeneration. During the regenerative phase, ex vivo or in vivo retroviral-mediated gene transfer into hepatocytes results in greater transduction efficiencies. The compns. and methods thus provide new means for gene therapy, and transgenic non-human animals useful in developing new therapeutic and preventative agents. The vectors can be used for high efficiency transduction of **ribozymes** specific for **hepatitis C virus** RNA.

L8 ANSWER 47 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 124:49498 CA
TITLE: RNA-cleaving compositions containing ribozymes and cell surface receptors-targeting agents
INVENTOR(S): Yamada, Shuhei; Kyozawa, Kyomichi
PATENT ASSIGNEE(S): Daiichi Kagaku Yakuhin Kk, Japan; Yamada Shuhei; Kyozawa Kyomichi
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07231784	A2	19950905	JP 1994-25110	19940223 <--

PRIORITY APPLN. INFO.:
JP 1994-25110 19940223

AB The compn. contg. (1) a ribozyme conjugated on both ends with 2 nucleotide fragments complementary to the RNA targets and (2) a (glyco)peptide ligand that has receptors on the target cell membrane surface, which (glyco)peptide is conjugated with a polycation via a linker. A

ribozyme capable of cleaving **hepatitis c virus** (HCV) RNA, which **ribozyme** is flanked with 2 oligonucleotides targeting the HCV core region is provided. An asialoorosomucoid conjugated with poly-(L)-lysine via a disulfide group is also provided for liver cells-specific introduction of the ribozyme through asialoglycoprotein receptors. Asialoglycoprotein receptors-mediated endocytosis of the ribozymes is demonstrated using human liver cell line HepG2. Cleavage of HCV RNA in human liver tumor cells is also shown.

L8 ANSWER 48 OF 55 CA COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 123:218380 CA
TITLE: **Ribozymes** cleaving **hepatitis C virus** RNA for inhibition of viral replication and treatment of hepatitis
INVENTOR(S): Draper, Kenneth G.
PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 100
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9519429	A2	19950720	WO 1995-US495	19950112 <--
WO 9519429	A3	19950908		
W: AU, CA, JP, KR, MX				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5610054	A	19970311	US 1994-182968	19940113 <--
AU 9515665	A1	19950801	AU 1995-15665	19950112 <--
EP 737247	A1	19961016	EP 1995-907430	19950112 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09508018	T2	19970819	JP 1995-519142	19950112 <--
AU 9851819	A1	19980611	AU 1998-51819	19980112 <--
AU 729657	B2	20010208		
AU 9939188	A1	19990916	AU 1999-39188	19990713 <--

PRIORITY APPLN. INFO.:

US 1994-182968	A	19940113
US 1992-882888	B2	19920514
WO 1995-US495	W	19950112
AU 1995-26422	A3	19950518
US 1996-623891	A	19960325

AB **Ribozymes** that cleave the RNA of **hepatitis C virus** to prevent replication are described for use in the treatment of the disease. Preferred targets for these ribozymes are the 5'-untranslated region and the genes for the C protein or NS3.

L8 ANSWER 49 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2000:390718 SCISEARCH
THE GENUINE ARTICLE: 315LG
TITLE: A study of **ribozyme** against **hepatitis C virus** in vitro
AUTHOR: Chen Z (Reprint); Liu Y; Liu K Z; Rh D N; Dou J; Reinhard U
CORPORATE SOURCE: ZHEJIANG MED UNIV, INST INFECT DIS, HANGZHOU 310003, PEOPLES R CHINA (Reprint); MED UNIV LUBECK, INST MICROBIOL, D-23538 LUBECK, GERMANY
COUNTRY OF AUTHOR: PEOPLES R CHINA; GERMANY
SOURCE: CHINESE MEDICAL JOURNAL, (**FEB 2000**) Vol. 113, No. 2, pp. 123-123.
Publisher: CHINESE MEDICAL ASSOCIATION, 42 DONGSI XIDAJIE,

BEIJING 100710, PEOPLES R CHINA.
ISSN: 0366-6999.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 0

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Objective To determine the nucleotide sites of hepatitis C virus (HCV), which can be cleaved by ribozymes, and to obtain a highly effective, nontoxic and inexpensive antisense ribozyme specific for HCV.

Methods Two effective ribozymes (HCRZNL and HCRZC), targeted to HCV 5' NC region and C region, were designed and synthesized. Eukaryotic expression vectors, pSV2-gpt, CD-SR alpha, containing either HCRZNC or HCRZC were constructed and transfected into MT-2 cells, which had been infected by HCV. Quantitative polymerase chain reaction (PCR) and hybridization were used to determine the effect of inhibition of HCV by ribozymes.

Results HCRZNC and HCRZC suppressed the replication of HCV by 54.7% and 62.1%, respectively. Furthermore, when both ribozymes were cotransfected into cells, they suppressed replication by 78.8%.

Conclusion The specific antisense ribozymes, have strong inhibitory effects on the replication of HCV in cultured cells, and have better effect when used together.

L8 ANSWER 50 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:877914 SCISEARCH
THE GENUINE ARTICLE: 239XE
TITLE: Optimization of synthetic stabilized **ribozymes** directed against **hepatitis C virus** RNA.
AUTHOR: Jamison S F (Reprint); VanCarlowitz I R; Macejak D G; Pavco P A; Roberts E C; Bellon L; Blatt L M
CORPORATE SOURCE: RIBOZYME PHARMACEUT, BOULDER, CO
COUNTRY OF AUTHOR: USA
SOURCE: HEPATOLOGY, (**OCT 1999**) Vol. 30, No. 4, Part 2, Supp. [S], pp. 1122-1122.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0270-9139.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L8 ANSWER 51 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:877786 SCISEARCH
THE GENUINE ARTICLE: 239XE
TITLE: Inhibition of viral replication by nuclease resistant hammerhead **ribozymes** directed against **hepatitis C virus** RNA.
AUTHOR: Macejak D J (Reprint); Jensen K L; Bellon L; Pavco P A; Blatt L M
CORPORATE SOURCE: RIBOZYME PHARMACEUT, BOULDER, CO
COUNTRY OF AUTHOR: USA
SOURCE: HEPATOLOGY, (**OCT 1999**) Vol. 30, No. 4, Part 2, Supp. [S], pp. 995-995.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0270-9139.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English

REFERENCE COUNT: 0

L8 ANSWER 52 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:877201 SCISEARCH
THE GENUINE ARTICLE: 239XE
TITLE: Tissue distribution of a **ribozyme** directed against **hepatitis C virus** RNA following subcutaneous or intravenous administration in mice.
AUTHOR: Lee P A (Reprint); Blanchard K S; Pavco P A; Sandberg J A; Bellon L; Blatt L M; Chlipala E; Bendele A M
CORPORATE SOURCE: RIBOZYME PHARMACEUT, BOULDER, CO; BOLDERPATH INC, BOULDER, CO
COUNTRY OF AUTHOR: USA
SOURCE: HEPATOLOGY, (**OCT 1999**) Vol. 30, No. 4, Part 2, Supp. [S], pp. 405-405.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0270-9139.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L8 ANSWER 53 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1998:789953 SCISEARCH
THE GENUINE ARTICLE: 125VQ
TITLE: Synthesis and testing of nuclease resistant hammerhead **ribozymes** directed against **hepatitis C virus** RNA.
AUTHOR: Roberts E C (Reprint); Malmstrom T A; Pavco P A; Domenico K K; Bellon L; Conrad A J; Tong M J; Blatt L M
CORPORATE SOURCE: HUNTINGTON MEM HOSP, PASADENA, CA; NATL INST GENET, LOS ANGELES, CA; RIBOZYME PHARMACEUT INC, BOULDER, CO
COUNTRY OF AUTHOR: USA
SOURCE: HEPATOLOGY, (**OCT 1998**) Vol. 28, No. 4, Part 2, Supp. [S], pp. 942-942.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0270-9139.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L8 ANSWER 54 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 96:763770 SCISEARCH
THE GENUINE ARTICLE: VL285
TITLE: COMPARISON OF 3 DIFFERENT HAMMERHEAD **RIBOZYMES** FOR CLEAVAGE EFFICIENCY OF **HEPATITIS-C VIRUS**-RNA IN-VITRO
AUTHOR: OHKAWA K (Reprint); YUKI N; KANAZAWA K; UEDA K; SASAKI Y; KASAHARA A; HAYASHI N
CORPORATE SOURCE: OSAKA UNIV, SCH MED, DEPT MED 1, SUITA, OSAKA 565, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: HEPATOLOGY, (**OCT 1996**) Vol. 24, No. 4, Part 2, Supp. S, pp. 1079.
ISSN: 0270-9139.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L8 ANSWER 55 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 95:702332 SCISEARCH
THE GENUINE ARTICLE: RX690
TITLE: INHIBITION OF **HEPATITIS-C VIRUS**-DIRECTED TRANSLATION BY HAMMERHEAD **RIBOZYMES** IN-VITRO
AUTHOR: SAKAMOTO N (Reprint); WU C H; WU G Y
CORPORATE SOURCE: UNIV CONNECTICUT, SCH MED, CTR HLTH, DEPT MED, DIV GASTROENTEROL HEPATOL, FARMINGTON, CT, 00000
COUNTRY OF AUTHOR: USA
SOURCE: HEPATOLOGY, (**OCT 1995**) Vol. 22, No. 4, Part 2, Supp. S, pp. 896.
ISSN: 0270-9139.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References